On Organic Compounds of Arsenic. Part II. Reaction between the Grignard Reagent and Arsenic Trioxide.

By

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ABSTRACT.

The action of arsenic trioxide on the Grignard reagent was studied. On treating arsenic trioxide with phenylmagnesium bromide, triphenylarsine and diphenylarsine oxide were obtained; with p-tolymagnesium bromide, tri-p-tolylarsine and di-p-tolylarsine oxide were isolated; with α-naphthylmagnesium bromide, di-α-naphthylarsine oxide was formed. On boiling the ethereal solution of methylmagnesium iodide with di-α-naphthylarsine oxide methyl-di-α-naphthylarsine was produced. From these facts, the authors have come to the conclusion that Sachs and Kantarowitz's view about the reaction (Ber., 41, 2767) is incorrect, and that the reaction should rather be regarded as taking place according to the following equation: $As_2O_3+4RMgBr=(R_2As)_2O+2MgO+2MgBr_2$; $(R_2As)_2O+2RMgBr=2R_3As+M_2O+MgBr_2$.

The following compounds were isolated and examined: di-α-naphthylarsine oxide $[(C_{10}H_7)_2As]_2O.H_2O$, white crystalline powder, M.P. 240–241°; di-α-naphthylarsine trichloride, $(C_{10}H_7)_2AsCl_3$, yellow crystalline powder; di-α-naphthylarsinic acid, $(C_{10}H_7)_2AsO.OH$, white amorphous powder, M.P. 228–229°; methyl-di-α naphthylarsine, $(C_{10}H_7)_2As.CH_3$, colourless needles, M. P. 145–146° and di-α-naphthylarsine oxychloride, $[(C_{10}H_7)_2AsCl_2)]_2O$.

The melting points of p-tolylarsine compounds were found as follows: tri-p-tolylarsine 146–147°, di-p-tolylarsine oxide 105–106° and di-p-tolylarsinic acid 173–174°.

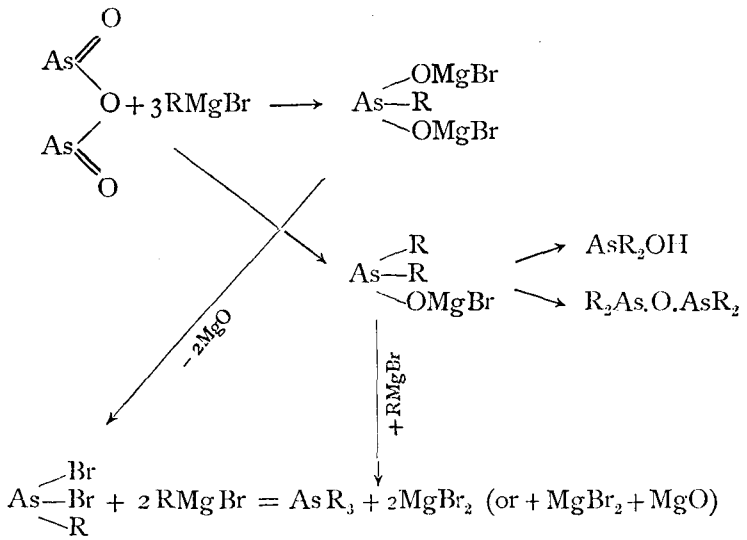
The action of the Grignard reagent on arsenic halide has been extensively employed in the synthesis of organic compounds of arsenic. In all these investigations, the reaction products obtained were always tertiary arsine, secondary arsine only having been obtained under special circumstances.[1]

Sachs and Kantarowitz[2] observed that finely powdered arsenic trioxide readily reacts with phenyl-, p-tolyl- and benzylmagnesium halide and

1 K. Matsumiya, These Memoirs, **4**, 217 (1920); C.A., **15**, 70 (1921).

2 Sachs and Kantarowitz, Ber., **41**, 2767 (1908).

gives diphenylarsine oxide, triphenylarsine, tri-p-tolylarsine and a compound of the composition, $(C_6H_5.CH_2)_2AsOH+H_2O$. They expressed the reaction by the following equation.



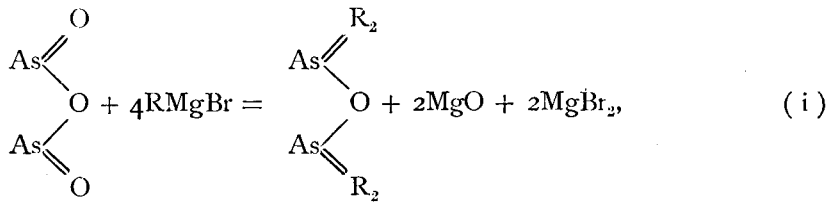
On repeating their experiments on the reaction of phenylmagnesium bromide under the same conditions we always obtained both diphenylarsine oxide and triphenylarsine, and could not confirm Sachs and Kantarowitz's statement that the former is the product at a lower temperature and the latter that at a higher. The only difference brought about by temperature was the relative quantities of two products; when long heated the quantity of tertiary arsine somewhat increased and that of diphenylarsine oxide decreased. With p-tolylmagnesium bromide di-p-tolylarsine oxide was produced together with tri-p-tolylarsine.

The action of α-naphthylmagnesium bromide on arsenic trioxide was also examined. In this reaction di-α-naphthylarsine oxide was produced in a good yield. No other product was isolated in spite of several trials.

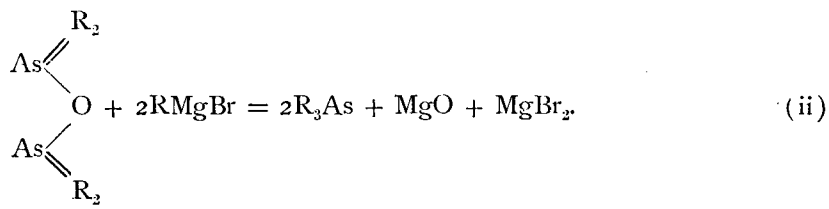
From the result of the above experiments, it may be assumed that the reaction between the Grignard reagent and arsenic trioxide primarily forms secondary arsine oxide, and then gives the tertiary arsine on the further action of the Grignard reagent.

Now, if Sachs and Kantarowitz's explanation is corrrect, the primary compound must generally be formed together with the secondary and tertiary ones, and it will be difficult to explain why in certain case no other arsine derivatives except the secondary are formed.

The authors, therefore, are of the opinion that the reaction takes place in two stages, as is expressed in the following equations:



$$\text{O}(\text{As}(=\text{O})\text{O}\text{As}(=\text{O}))\text{O} + 4\text{RMgBr} = \text{R}_2\text{As}(\text{O}\text{As}(=\text{O})\text{O})\text{AsR}_2 + 2\text{MgO} + 2\text{MgBr}_2, \qquad \text{(i)}$$



$$\text{R}_2\text{As}(\text{O}\text{As}(=\text{O})\text{O})\text{AsR}_2 + 2\text{RMgBr} = 2\text{R}_3\text{As} + \text{MgO} + \text{MgBr}_2. \qquad \text{(ii)}$$

To see whether the reaction (ii) takes place with α-naphthylmagnesium bromide or not, it was treated with a large excess of the Grignard reagent; the result was negative. Di-α-naphthylarsine oxide was then boiled for several hours with α-naphthylmagnesium bromide freshly prepared, but no reaction took place. From these experiments, α-naphthylmagnesium bromide was thought to be too feeble to attack di-α-naphthylarsine oxide. When methylmagnesium iodide was used in place of α-naphthylmagnesium bromide the reaction set in smoothly and methyl-di-α-naphthylarsine was produced as was expected.

$$[(\text{C}_{10}\text{H}_7)_2\text{As}]_2\text{O} + 2\text{CH}_3\text{MgI} = 2(\text{C}_{10}\text{H}_7)_2\ \text{As.CH}_3 + \text{MgO} + \text{MgI}_2.$$

Since di-α-naphthylarsine compound is hitherto little known, some experiments were conducted to prepare some of its derivatives. Di-α-naphthylarsine oxide was first transformed into di-α-naphthylchloroarsine by treating it with methyl alcoholic hydrochloric acid, and the product was found identical with that prepared from α-naphthylmagnesium bromide and arsenic trichloride.[1] Di-α-naphthylchloroarsine was then transformed back to di-α-naphthylarsine oxide by treating it with an alcoholic potash. By passing chlorine gas into the ethereal solution of di-α-naphthylchloroarsine, di-α-naphthylarsine trichloride was isolated as a yellow crystalline powder which is easily decomposed by atmospheric moisture. The

1 K. Matsumiya, These Memoirs, *loc. cit.*

trichloride easily hydrolyses into di-α-naphthylarsinic acid, which is also obtained by treating di-α-naphthylarsine oxide with chlorine and subsequently with water. The yellow crystals intermediately formed by the action of chlorine upon di-α-naphthylarsine oxide were isolated and analysed. Their composition was $[(C_{10}H_7)_2AsCl_2]_2O$.

EXPERIMENTAL PART.

1. *Action of Phenylmagnesium Bromide upon Arsenic Trioxide.*

i) To the ethereal solution of phenylmagnesium bromide prepared from 31·4 grm. ($\frac{1}{5}$ mol.) of bromobenzene, 5 grm. ($\frac{1}{5}$ mol.) of magnesium and a piece of iodine, 10 grm. ($\frac{1}{20}$ mol.) of powdered arsenic trioxide were gradually added, being cooled all the time, and the mixture was boiled for 3 hours on a water-bath. Then the reaction product was cautiously treated with water and dilute acetic acid. After distilling off the ether and diphenyl, the residue was extracted with ether, and the ethereal solution was dried with anhydrous sodium sulphate. After the ether had been removed, a yellowish tarry substance which solidified gradually on standing was obtained. It was pressed between clean filter-papers to remove the yellowish tarry matter and then washed with a small quantity of alcohol. On recrystallising it from alcohol repeatedly, colourless crystals melting at 91–92°[1] were obtained. The yield was 8 grm. Its analytical results were as follows:—

0·1370 grm. of the sample required 23 c.c. of $\frac{N}{20}$ iodine solution.

0·1590 grm. substance gave 0·3535 grm. CO_2 and 0·0649 grm. H_2O.

	Calc. for $[(C_6H_5)_2As]_2O$	Found
As	31·62	31·48
C	60·75	60·63
H	4·26	4·58

The yellow oily matter retained in the filter-papers was extracted with ether and treated with an ethereal solution of mercuric chloride[2] until a white precipitate ceased to be produced. The mercurichloride was dissolved in boiling alcohol and then treated with hydrogen sulphide,

1 La Coste and Michaelis, Ann., **201**, 229 (1880); Sachs and Kantarowitz, *loc. cit.*

2 La Coste and Michaelis, *ibid.*, 241.

whereby mercuric sulphide was instantly precipitated. From the alcoholic solution, colourless crystals were obtained which, after repeated recrystallisation from alcohol, melted at 58–60°.[1] The yield was 2 grm. Arsenic was determined by Ewin's method with the following result:—

0·1604 grm. substance required 20·8 c.c. of $\frac{N}{20}$ iodine solution.

	Calc. for $(C_6H_5)_3As$	Found
As	24·49	24·32

The ethereal solution containing mercuric chloride was repeatedly shaken with dilute hydrochloric acid and then saturated with chlorine, when a slightly yellow-coloured precipitate was formed. It was treated with a dilute caustic soda solution and decolourlised with animal charcoal. On acidifying the solution with hydrochloric acid, almost colourless crystals were separated. They were recrystallised from water and then from ether. Colourless crystals thus obtained melted at 170–171°.[2] The yield was 1·6 grm. The analytical result was as follows:—

0·1480 grm. substance required 22·45 c.c of $\frac{N}{20}$ iodine solution.

	Calc. for $(C_6H_5)_2AsO.OH$	Found
As	28·61	28·44

ii) Experiments conducted under the same conditions as above, but without heating the mixture of arsenic trioxide and phenylmagnesium bromide gave nearly the same result, except that the yield of triphenylarsine more or less decreased and that of diphenylarsine oxide increased.

2. *Action of p-Tolylmagnesium Bromide upon Arsenic Trioxide.*

To the Grignard reagent prepared from 9 grm. ($\frac{1}{20}$ mol.) of p-bromotoluene, 1·3 grm. ($\frac{1}{20}$ mol.) of magnesium and a trace of methyl iodide in 30 c.c of dry ether, 2·5 grm. ($\frac{1}{80}$ mol.) of arsenic trioxide were gradually added, with frequent shaking and cooling. The reaction product was boiled for 30 minutes on a water-bath and left to stand over night. Then it was decomposed with water and dilute acetic acid. Ether and di-p-tolyl were removed by steam distillation and the residue was extracted with ether. The ether extract was treated with an ethereal

1 La Coste and Michaelis, *loc. cit.*, 237; Michaelis, Ann., **321**, 160 Sachs and Kantarowitz, *loc cit.*

2 La Coste and Michaelis, *ibid.*, 231.

solution of mercuric chloride, when tri-p-tolylarsine was precipitated as mercurichloride.[1]

This mercurichloride was dissolved in boiling alcohol and treated with alcoholic potash. The mercuric oxide formed was removed and carbon dioxide was passed into the filtered alcoholic solution to remove the excess of caustic potash. On evaporating the alcoholic solution, a slightly brown-coloured residue was obtained. It was extracted with ether and recrystallised from the same solvent, when colourless crystals melting at 146–147° were obtained (M. P. of tri-p-tolylarsine is given by La Coste and Michaelis as 145–146°[2]). The yield was 0·3 grm. It was analysed with the following result.

0·1637 grm. substance required 18·82 c.c of $\frac{N}{20}$ iodine solution.

	Calc. for $(CH_3 \cdot C_6H_4)_3$ As	Found
As	21·53	21·56

The ethereal solution containing mercuric chloride was washed well with dilute hydrochloric acid to remove the excess of mercuric chloride, and dried with sodium sulphate. On evaporating ether, fine needle crystals and a small quantity of yellowish oily matter were obtained.

The needle crystals, removed from the oily matter by washing with ether, and recrystallised from ether, melted at 105–106° (M. P. of di-p-tolylasine oxide given by La Coste is 69°[3]). The yield was 0·7 grm. Analysis gave the following results:—

0·1337 grm. substance required 20·94 c.c. of $\frac{N}{20}$ iodine solution.

0·1643 grm. substance gave 0·3804 grm. CO_2 and 0·0804 grm. H_2O.

	Calc. for $[(CH_3 \cdot C_6H_4)_2$ As$]_2O$	Found
As	28·28	28·00
C	63·38	63·16
H	5·32	5·48

The ethereal washing containing the oily matter was saturated with chlorine gas, and a slightly yellow-coloured precipitate was obtained. It was dissolved in a dilute caustic soda solution and decolourlised with animal charcoal. On acidifying the alkaline solution with hydrochloric acid, colourless crystals were obtained, which after recrystallisation from hot

1 Michaelis, *loc. cit.*, 202.

2 La Coste, Ann., **208**, 26; Michaelis, *loc. cit.*, 200.

3 La Coste, *ibid.*, 19.

water melted at 173-174° (167° for di-p-tolyarsinic acid by La Coste[1]). The yield was 0·4 grm.

0·1402 grm. substance required 19·1 c.c of $\frac{N}{20}$ iodine solution.

	Calc. for $(CH_3{\cdot}C_5H_4)_2$ AsO.OH	Found
As	25·84	25·61

3. *Action of α-Naphthylmagnesium Brom upon Arsenic Trioxide.*

To the Grignard reagent prepared from 41·4 grm. ($\frac{1}{5}$ mol.) of α-bromonaphthalene, 5 grm. ($\frac{1}{5}$ mol.) of magnesium and a piece of iodine in 60 c.c. of dry ether, 40 grm. ($\frac{1}{5}$ mol.) of arsenic trioxide were gradually added and the mixture was boiled for 30 minutes on a water-bath. Then it was treated with water and dilute acetic acid and subjected to steam distillation to remove ether and naphthalene. The purification of the product was no easy task, as some colouring substance could not be completely removed even after several recrystallisations. The following method of purification was, however, found very effective. The solid substance was washed well with ether and then was introduced into a Soxlet tube and extracted with carbon bisulphide. From this carbon bisulphide extract a slightly yellow coloured powder was obtained which was again introduced into the Soxlet tube and treated with ether so as to remove coloured impurities. Thus a white powder melting at 240-241° was obtained. The yield ammounted to 11 grms. The results of analysis were as follows:—

0·1726 grm. substance required 19·97 c.c of $\frac{N}{20}$ iodine solution.

0·2527 grm. of the sample gave 0·6449 grm. CO_2 and 0·1031 grm. H_2O.

	Calc. for $[(C_{10}H_7)_2As]_2O.H_2O$ or $(C_{10}H_7)_2AsOH$	Found
As	21·66	21·70
C	69·35	69·61
H	4·37	4·57

Di-α-naphthylarsine oxide is a white crystalline powder. It is insoluble in ether and alcohol, slightly soluble in hot benzene, chloroform and carbon tetrachloride and easily soluble in carbon bisulphide.

1 La Coste, *loc. cit.*, 20.

4. *Action of α-Naphthylmagnesium Bromide upon Di-α-naphthylarsine Oxide.*

All attempts to bring α-naphthylmagnesium bromide and arsenic trioxide into reaction failed and no other organic compound of arsenic except di-α-naphthylarsine oxide could be isolated. Di-α-naphthylarsine oxide was boiled for several hours with an ethereal solution of α-naphthylmagnesium bromide. But this also gave no result.

5. *Action of Methylmagnesium Iodide upon Di-α-naphthylarsine Oxide.*

To the grignard reagent prepared from 5·6 grm. ($\frac{1}{25}$ mol.) of methyl iodide and 1 grm. ($\frac{1}{25}$ mol.) of magnesium in dry ether, 2·2 grm. ($\frac{1}{100}$ mol.) of di-α-naphthylarsine oxide were added and the mixture was boiled for 8 hours on a water-bath. The reaction product was decomposed with water and dilute. acetic acid, and subjected to steam distillation. The residue was extracted with ether, and the solid left on evaporation of the solvent was recrystallised to colourless needles from benzene-alcohol. They melted at 145–146° and the yield was 0·7 grm. The analytical result was as follows:—

0·1475 grm. substance required 16·9 c.c of $\frac{N}{20}$ iodine solution.

	Calc. for $(C_{10}H_7)_2As.CH_3$	Found
As	21·78	21·48

Methyl-di-α-naphthylarsine forms colourless fine needles. It is slightly soluble in alcohol and easily soluble in other ordinary organic solvents.

6. *Action of Methyl Alcoholic Hydrochloric Acid upon Di-α-naphthylarsine oxide.*

Three grms. of di-α-naphthylarsine oxide and 50 c.c of 20% methyl alcoholic hydrochloric acid were boiled for an hour on a water-bath under a reflux condenser. After evaporation of the solvent a brownish residue was obtained. It was dissolved in a small quantity of benzene and then ether was added to the benzene solution. The precipitates instantly formed thus were recrystallised from benzene-alcohol. Yellowish crystals melting at 166–167°[1] were obtained with a quantitative yield. They were analysed with the following results:—

1 K. Matsumiya, These Memoirs, *loc. cit.*

0·1205 grm. substance required 13·27 c.c of $\frac{N}{20}$ iodine solution.

0·1261 grm. of the sample required 51·6 c.c of $\frac{N}{20}$ potassium thiocynide solution.

	Calc. for $(C_{10}H_7)_2AsCl$	Found
As	20·56	20·65
Cl	9·73	9·54

7. *Action of Alcoholic Potash upon Di-α-naphthylchloroarsine (Di-α-naphthylarsenious Chloride).*

Freshly prepared alcoholic potash was slowly added to a boiling alcoholic solution of di-α-naphthylchloroarsine until the solution became distinctly alkaline. The reaction product was diluted with water and filtered, and the residue was washed well with water until the washing no longer gave an alkaline reaction. Then it was extracted with ether in a Soxlet tube, and a white crystalline powder melting at 240–241° was produced. The results of analysis were as follows:—

0·1742 grm. substance gave 0·4430 grm. CO_2 and 0·0742 grm. H_2O.

0·1453 grm. substance required 16·84 c.c of $\frac{N}{20}$ iodine solution.

	Calc. for $[(C_{10}H_7)_2As]_2O.H_2O$ or $(C_{10}H_7)_2AsOH$	Found
As	21·66	21·73
C	69·35	49·36
H	4·37	4·77

8. *Action of Chlorine upon Di-α-naphthylchloroarsine.*

Dry chlorine gas was passed into di-α-naphthylchloroarsine suspended in absolute ether, whereby a yellow precipitate was produced. Ether was decanted and the precipitate was cautiously washed with absolute ether and dried by passing dry air over it. It was analysed with the following results:—

0·1742 grm. substance required 16·35 c.c of $\frac{N}{20}$ iodine solution.

0·0909 grm. substance gave 0·0910 grm. AgCl.

	Calc. for $(C_{10}H_7)_2AsCl_3$	Found
As	17·22	17·60
Cl	24·43	24·76

Di-α-naphthylarsine trichloride is a yellow-coloured crystalline powder. It is very hygroscopic and instantly hydrolyses in moist air and becomes white.

9. *Action of Water upon Di-α-naphthylarsine Trichloride.*

Di-α-naphthylarsine trichloride was treated with water and the white precipitate formed was washed well with water. An amorphous white powder melting at 228–229° was finally obtained after several recrystallisations from benzene-ether solution. Its analysis gave the following results:—

0·1519 grm. of the sample required 16·8 c.c of $\frac{N}{20}$ iodine solution.

0·1721 grm. substance gave 0·4183 grm. CO_2 and 0·0690 grm. H_2O.

	Calc. for $(C_{10}H_7)_2AsO.OH$	Found
As	20·70	20·74
C	66·28	66·30
H	4·18	4·49

Di-α-naphthylarsinic acid is easily soluble in alcohol, chloroform, benzene and alkali, insoluble in ether, carbon bisulphide and water.

10. *Action of Chlorine upon Di-α-naphthylarsine Oxide.*

To di-α-naphthylarsine oxide suspended in absolute ether, dry chlorine gas was introduced. Then yellow coloured precipitates were produced. The solvent was decanted off and the residue was carefully washed with absolute ether two or three times. It was dried in a current of dry air and then kept in vacuum over sulphuric acid. Arsenic and chlorine were determined as follows:—

0·1596 grm. substance required 15·1 c.c of $\frac{N}{20}$ iodine solution.

0·0960 grm. of the sample gave 0·0660 grm. AgCl.

	Calc. for $[(C_{10}H_7)_2AsCl_2]_2O$	Found
As	18·37	17·74
Cl	17·38	17·00

Di-α-naphthylarsine oxychloride is a yellow crystalline powder which is easily decomposed even in a moist atmosphere.

11. *Action of Water upon Di-α-naphthylarsine Oxychloride.*

Di-α-naphthylarsine oxychloride was treated with water, and a white substance thus formed was repeatedly recrystallised from benzene-ether solution. A white amorphous powder melting at 228–229° was obtained. It was analysed and the arsenic content was determined.

0·1476 grm. substance required 16·25 c.c of $\frac{N}{20}$ iodine solution.

	Calc. for $(C_{10}H_7)_2AsO.OH$	Found
As	20·70	20·64